```
FILE 'REGISTRY' ENTERED AT 13:18:35 ON 12 MAY 2005

=> S NUCLEASE/CN
L1             1 NUCLEASE/CN

FILE 'CAPLUS' ENTERED AT 13:19:00 ON 12 MAY 2005

=> S L1;S NUCLEASE;S L2,L3;S CHIMERIC;S L5(3A)L4
L2          2517 L1


          20347 NUCLEASE
           6185 NUCLEASES
L3         24458 NUCLEASE
                 (NUCLEASE OR NUCLEASES)


L4         24536 (L2 OR L3)

          43553 CHIMERIC
             29 CHIMERICS
L5         43564 CHIMERIC
                 (CHIMERIC OR CHIMERICS)


L6            49 L5(3A)L4

=> S CLEAVAGE;S BINDING;S L6 AND (L7,L8)
         199457 CLEAVAGE
           5291 CLEAVAGES
L7       201957 CLEAVAGE
                 (CLEAVAGE OR CLEAVAGES)


         867419 BINDING
           1905 BINDINGS
L8       867955 BINDING
                 (BINDING OR BINDINGS)


L9            28 L6 AND ((L7 OR L8))

=> S REPAIR SUBSTRATE
          74292 REPAIR
           3240 REPAIRS
          76123 REPAIR
                 (REPAIR OR REPAIRS)
         800804 SUBSTRATE
         368005 SUBSTRATES
        1000821 SUBSTRATE
                 (SUBSTRATE OR SUBSTRATES)
L10           42 REPAIR SUBSTRATE
                 (REPAIR(W)SUBSTRATE)

=> S L10 AND L6
L11            0 L10 AND L6

=> S L10,L6
L12           91 (L10 OR L6)

=> S L12 NOT L10
L13           49 L12 NOT L10
```

=> D L10 1-28 CBIB ABS;D L13 1-49 TI

L10 ANSWER 1 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2005:309129 SUMO Modification: Wrestling with Protein Conformation. Ulrich, Helle D. (Cancer Research UK, Clare Hall Laboratories, South Mimms, EN6 3LD, UK). Current Biology, 15(7), R257-R259 (English) 2005. CODEN: CUBLE2. ISSN: 0960-9822. Publisher: Cell Press.
AB SUMO modification of human thymine-DNA glycosylase facilitates the processing of base excision repair substrates by an unusual mechanism: while leaving the catalytic center unaffected, it induces product release by eliciting a conformational change in the enzyme.

L10 ANSWER 2 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2004:1066668 Document No. 142:213220 Double-strand break repair machinery is sensitive to UV radiation. Ilnytskyy, Yaroslav; Yao, Youli; Kovalchuk, Igor (Department of Biological Sciences, University of Lethbridge, Lethbridge, AB, T1K 3M4, Can.). Journal of Molecular Biology, Volume Date 2005, 345(4), 707-715 (English) 2004. CODEN: JMOBAK. ISSN: 0022-2836. Publisher: Elsevier B.V..
AB The precision of the repair of linearized plasmid DNA was analyzed using a nonsense mutation inactivated β-glucuronidase (uidA) marker gene delivered to Nicotiana plumbaginifolia protoplasts and Nicotiana tabacum leaves. The reversions at the stop-codon allowed the reactivation of the marker gene. Here we report that irradiation of plant protoplasts or plant tissue prior to the delivery of the DNA repair substrate significantly potentiated the reversion frequency leading to a two to fourfold increase over the non-irradiated samples. The increase in reversion frequency was highest upon the delivery of the linear substrates, suggesting increased sensitivity of the double-strand break (DSB) repair apparatus to UV-C. Moreover, the most significant UV irradiation effect was observed in plasmids linearized in close proximity to the stop codon. The higher reversion frequency in UV-treated samples was apparently due to the involvement of free radicals as pretreatment of irradiated tissue with radical scavenging enzyme N-acetyl--cysteine abolished the effect of UV-C. We discuss the UV-sensitivity of various repair enzymes as well as possible mechanisms of involvement of error-prone polymerases in processing of DSBs.

L10 ANSWER 3 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2004:538096 Document No. 141:220455 Substrate specificities of bacterial and human AlkB proteins. Falnes, Pal O.; Bjoras, Magnar; Aas, Per Arne; Sundheim, Ottar; Seeberg, Erling (Centre for Molecular Biology and Neuroscience, Institute of Medical Microbiology, Rikshospitalet University Hospital, Oslo, 0027, Norway). Nucleic Acids Research, 32(11), 3456-3461 (English) 2004. CODEN: NARHAD. ISSN: 0305-1048. Publisher: Oxford University Press.
AB Methylating agents introduce cytotoxic 1-methyladenine (1-meA) and 3-methylcytosine (3-meC) residues into nucleic acids, and it was recently demonstrated that the Escherichia coli AlkB protein and two human homologs, hABH2 and hABH3, can remove these lesions from DNA by oxidative demethylation. Moreover, AlkB and hABH3 were also found to remove 1-meA and 3-meC from RNA, suggesting that cellular RNA repair can occur. We have here studied the preference of AlkB, hABH2 and hABH3 for single-stranded DNA (ssDNA) or double-stranded DNA (dsDNA), and show that AlkB and hABH3 prefer ssDNA, while hABH2 prefers dsDNA. This was consistently observed with three different oligonucleotide substrates, implying that the specificity for single-stranded vs. double-stranded DNA is sequence independent. The dsDNA preference of hABH2 was observed only in the presence of magnesium. The activity of the enzymes on single-stranded RNA (ssRNA), double-stranded RNA (dsRNA) and DNA/RNA hybrids was also investigated, and the results generally confirm the notion that while AlkB and hABH3 tend to prefer single-stranded nucleic acids, hABH2 is more active on

double-stranded substrates. These results may contribute to identifying the main substrates of bacterial and human AlkB proteins in vivo.

L10 ANSWER 4 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2004:307020 Document No. 141:34486 Modulation of error-prone double-strand break repair in mammalian chromosomes by DNA mismatch repair protein Mlh1. Bannister, Laura A.; Waldman, Barbara Criscuolo; Waldman, Alan S. (Department of Biological Sciences, University of South Carolina, Columbia, SC, 29208, USA). DNA Repair, 3(5), 465-474 (English) 2004. CODEN: DRNEAR. ISSN: 1568-7864. Publisher: Elsevier Science B.V..

AB We assayed error-prone double-strand break (DSB) repair in wild-type and isogenic Mlh1-null mouse embryonic fibroblasts containing a stably integrated DSB repair substrate. The substrate contained a thymidine kinase (tk) gene fused to a neomycin-resistance (neo) gene; the tk-neo fusion gene was disrupted in the tk portion by a 22 bp oligonucleotide containing the 18 bp recognition site for endonuclease I-SceI. Following DSB-induction by transient expression of I-SceI endonuclease, cells that repaired the DSB by error-prone nonhomologous end-joining (NHEJ) and restored the correct reading frame to the tk-neo fusion gene were recovered by selecting for G418-resistant clones. The number of G418-resistant clones induced by I-SceI expression did not differ significantly between wild-type and Mlh1-deficient cells. While most DSB repair events were consistent with simple NHEJ in both wild-type and Mlh1-deficient cells, complex repair events were more common in wild-type cells. Furthermore, genomic deletions associated with NHEJ events were strikingly larger in wild-type vs. Mlh1-deficient cells. Addnl. expts. revealed that the stable transfection efficiency of Mlh1-null cells is higher than that of wild-type cells. Collectively, our results suggest that Mlh1 modulates error-prone NHEJ by inhibiting the annealing of DNA ends containing noncomplementary base pairs or by promoting the annealing of microhomologies.

L10 ANSWER 5 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2004:290749 Document No. 141:4018 Defective DNA Repair as a Potential Mechanism for the Rapid Development of Drug Resistance in Plasmodium falciparum. Trotta, Richard F.; Brown, Matthew L.; Terrell, James C.; Geyer, Jeanne A. (Infectious Disease Service Department of Medicine, Walter Reed Army Medical Center, Washington, DC, 20307-5001, USA). Biochemistry, 43(17), 4885-4891 (English) 2004. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.

AB The development and spread of highly drug-resistant parasites pose a central problem in the control of malaria. Understanding mechanisms that regulate genomic stability, such as DNA repair, in drug-resistant parasites and during drug treatment may help determine whether this rapid onset of resistance is due to an increase in the rate at which resistance-causing mutations are generated. This is the first report to demonstrate DNA repair activities from the malaria-causing parasite Plasmodium falciparum that are specific for UV light-induced DNA damage. The efficiency of DNA repair differs dramatically among P. falciparum strains with varying drug sensitivities. Most notable is the markedly reduced level of repair in the highly drug-resistant W2 isolate, which has been shown to develop resistance to novel drugs at an increased rate when compared to drug-sensitive strains. Addnl., the antimalarial drug chloroquine and other quinoline-like compds. interfered with the DNA synthesis step of the repair process, most likely a result of direct binding to repair substrates. We propose that altered DNA repair, either through defective repair mechanisms or drug-mediated inhibition, may contribute to the accelerated development of drug resistance in the parasite.

L10 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2004:96997 Document No. 140:283290 Substrate Discrimination by Formamidopyrimidine-DNA Glycosylase: A mutational analysis. Zaika, Elena I.; Perlow, Rebecca A.; Matz, Eileen; Broyde, Suse; Gilboa, Rotem;

Grollman, Arthur P.; Zharkov, Dmitry O. (Department of Pharmacological Sciences, Laboratory of Chemical Biology, State University of New York at Stony Brook, Stony Brook, NY, 11794, USA). Journal of Biological Chemistry, 279(6), 4849-4861 (English) 2004. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Formamidopyrimidine-DNA glycosylase (Fpg) is a primary participant in the repair of 8-oxoguanine, an abundant oxidative DNA lesion. Although the structure of Fpg has been established, amino acid residues that define damage recognition have not been identified. The authors have combined mol. dynamics and bioinformatics approaches to address this issue. Site-specific mutagenesis coupled with enzyme kinetics was used to test the authors' predictions. On the basis of mol. dynamics simulations, Lys-217 was predicted to interact with the O8 of extrahelical 8-oxoguanine accommodated in the binding pocket. Consistent with the authors' computational studies, mutation of Lys-217 selectively reduced the ability of Fpg to excise 8-oxoguanine from DNA. Dihydrouracil, also a substrate for Fpg, served as a nonspecific control. Other residues involved in damage recognition (His-89, Arg-108, and Arg-109) were identified by combined conservation/structure anal. Arg-108, which forms two hydrogen bonds with cytosine in Fpg-DNA, is a major determinant of opposite-base specificity. Mutation of this residue reduced excision of 8-oxoguanine from thermally unstable mispairs with guanine or thymine, while excision from the stable cytosine and adenine base pairs was less affected. Mutation of His-89 selectively diminished the rate of excision of 8-oxoguanine, whereas mutation of Arg-109 nearly abolished binding of Fpg to damaged DNA. Taken together, these results suggest that His-89 and Arg-109 form part of a reading head, a structural feature used by the enzyme to scan DNA for damage. His-89 and Lys-217 help determine the specificity of Fpg in recognizing the oxidatively damaged base, while Arg-108 provides specificity for bases positioned opposite the lesion.

L10 ANSWER 7 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN

2004:94586 Document No. 140:316056 High frequency of nucleotide misincorporations upon the processing of double-strand breaks. Kovalchuk, Igor; Pelczar, Pawel; Kovalchuk, Olga (Department of Biological Sciences, University of Lethbridge, Lethbridge, AB, T1K 3M4, Can.). DNA Repair, 3(3), 217-223 (English) 2004. CODEN: DRNEAR. ISSN: 1568-7864. Publisher: Elsevier Science B.V..

AB Base substitutions were detected as a consequence of double-strand break (DSB) repair in plants. The fidelity of processing free DNA ends was analyzed using a stop-codon inactivated β-glucuronidase (uidA) reporter gene. Circular and linear plasmids carrying the inactive gene were delivered to Nicotiana plumbaginifolia protoplasts or Nicotiana tabacum leaves. Processing of breaks which occurred in close proximity (5-9 bp) to termination codons led to occasional reversions and subsequent gene reactivation. In contrast, the repair of breaks occurring at a greater distance from the stop-codon resulted in a significantly lower number of reversions. The data suggest that the error prone processing of the free ends involves partial degradation and re-synthesis of the DNA repair substrate.

L10 ANSWER 8 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN

2003:998322 Document No. 140:230365 High G/C content of cohesive overhangs renders DNA end joining Ku-independent. Sandoval, Ana; Labhart, Paul (Torrey Pines Institute for Molecular Studies, San Diego, CA, 92121, USA). DNA Repair, 3(1), 13-21 (English) 2004. CODEN: DRNEAR. ISSN: 1568-7864. Publisher: Elsevier Science B.V..

AB Ku plays an important role in the repair of double strand DNA breaks by non-homologous DNA end joining (NHEJ). Ku is thought to exert its function by aligning the two DNA ends. A previous study showed that the joining of certain cohesive DNA ends in cell-free in vitro reactions was independent of Ku [Mol. Cell. Biol. 19 (1999) 2585]. To investigate a possible correlation between Ku-dependence of DNA end joining reactions and the strength of base pair interactions between cohesive ends, we constructed a series of repair substrates

with either 3'- or 5'-overhangs, which consisted entirely of either A/T or G/C residues. We found that after Ku-immunodepletion of the extract, the joining of cohesive ends that associate by the formation of four A:T base pairs was reduced, while the joining of ends that associate through four G:C base pairs was unaffected or slightly stimulated. The precision of the repair was not reduced in Ku-independent reactions. Our results indicate that the requirement for Ku is dependent on how stably the two cohesive DNA ends can associate by base-pairing. Two independent assays for protein-DNA interactions did not reveal any differences in Ku binding to substrates with A/T and G/C overhangs, suggesting that in this system Ku is recruited to the repair site regardless of whether it is functionally required or not. The finding that Ku is dispensable for efficient and precise joining of ends with cohesive G/C overhangs also suggests that alignment of DNA ends may be the sole function of Ku during NHEJ.

L10 ANSWER 9 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2003:684870 Document No. 139:302888 Fidelity of primate cell repair of a double-strand break within a (CTG)·(CAG) tract: effect of slipped DNA structures. Marcadier, Julien L.; Pearson, Christopher E. (Department of Molecular & Medical Genetics, University of Toronto, Ontario, M5G 1X8, Can.). Journal of Biological Chemistry, 278(36), 33848-33856 (English) 2003. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB At least 15 human diseases are caused by the instability of gene-specific (CTG)·(CAG) repeats. The precise mechanism of instability remains unknown, though bacterial and yeast models have suggested a role for aberrant repair of double-strand breaks (DSBs). Using an established primate DSB repair system, we have investigated the fidelity of repair of a DSB within a (CTG)·(CAG) repeat tract. DSB repair substrates were generated from plasmids that are stably replicated in their circular form, permitting us to highlight the effects of DSB repair on repeat stability and minimize the contribution of replication. DSBs were introduced into repeat-containing plasmids using a unique BsmI site, such that the entire repeat tract comprised one free end of the linearized plasmid. Substrates containing 17, 47, and 79 repeats, in either their linear duplex form or containing slipped structures (out-of-register interstrand mispairings at repeat sequences), were transiently transfected into primate cells. Linearized plasmids with repeats were repaired with mildly reduced efficiency, while the presence of slipped structures considerably reduced repair efficiency. The repaired products were characterized for alterations within the repeat tract and flanking sequence. DSB repair induced predominantly repeat deletions. Notably, a polarized/directional deletion effect was observed, in that the repetitive end of the DSB was preferentially removed. This phenomenon was dramatically enhanced when slipped structures were present within the repeat tract, providing the first evidence for error-prone processing of slipped-strand structures. These results suggest the existence of primate nuclease activities that are specific for (CTG)·(CAG) repeats and the structures they form.

L10 ANSWER 10 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2002:928054 Document No. 138:14722 Process for multilayer coating of substrates. Awokola, Morenike; Flosbach, Carmen; Loffler, Helmut (Germany). U.S. Pat. Appl. Publ. US 2002182330 A1 20021205, 6 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-873714 20010604.

AB The invention is directed to a process for multilayer coating of substrates which comprises (a) applying a filler layer of a filler coating composition to a substrate, (b) curing the resultant filler layer by irradiation with high energy radiation and (c) applying a top coat layer to the cured filler layer and curing the top coat layer. The filler coating composition comprises (A) at least one binder capable of free-radical polymerization having fewer than three olefinic double bonds per mol., (B) at least one ester of alpha,beta-olefinically unsatd. monocarboxylic acids capable of free-radical polymerization having one olefinic double bond per mol. and (C) at least one compound having at least one phosphoric

acid group. The process applies to repair coatings, particularly in the fields of automotive and industrial coatings.

L10 ANSWER 11 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2002:612689 Document No. 137:245096 Down-regulation of DNA repair synthesis at DNA single-strand interruptions in poly(ADP-ribose) polymerase-1 deficient murine cell extracts. Sanderson, Russell J.; Lindahl, Tomas (Clare Hall Laboratories, Cancer Research UK London Research Institute, South Mimms, EN6 3LD, UK). DNA Repair, 1(7), 547-558 (English) 2002. CODEN: DRNEAR. ISSN: 1568-7864. Publisher: Elsevier Science B.V.
AB The functional involvement of poly(ADP-ribose) polymerase-1 (PARP-1) in the repair of DNA single- and double-strand breaks, DNA base damage, and related repair substrate intermediates remains unclear. Using an in vitro DNA repair assay and cell exts. derived from PARP-1 deficient or wild-type murine embryonic fibroblasts, we investigated the DNA synthesis and ligation steps associated with the rejoining of DNA single-strand interruptions containing 3'-OH, and either 5'-OH or 5'-P termini. Complete repair leading to DNA rejoining was similar between PARP-1 deficient cells and wild-type controls and poly(ADP-ribose) synthesis was, as expected, greatly reduced in PARP-1 deficient cell exts. The incorporation of [32P]dCMP into repaired DNA at the site of a lesion was reduced two-three-fold in PARP-1 deficient cell exts., demonstrating a decrease in repair patch size. Addition of purified PARP-1 to levels approximating those present in wild-type exts. did not stimulate DNA repair synthesis. We conclude that PARP-1 is not required for the efficient processing and rejoining of single-strand interruptions with defined 3'-OH and 5'-OH or 5'-P termini. Decreased DNA repair synthesis observed in PARP-1 deficient cell exts. is associated with reduced cellular expression of several factors required for long-patch base excision repair (BER), including FEN-1 and DNA ligase I.

L10 ANSWER 12 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2002:552634 Document No. 137:259225 Substrate Recognition by a Family of Uracil-DNA Glycosylases: UNG, MUG, and TDG. Liu, Pingfang; Burdzy, Artur; Sowers, Lawrence C. (Department of Biochemistry and Microbiology, School of Medicine, Loma Linda University, Loma Linda, CA, 92350, USA). Chemical Research in Toxicology, 15(8), 1001-1009 (English) 2002. CODEN: CRTOEC. ISSN: 0893-228X. Publisher: American Chemical Society.
AB In response to continuous hydrolytic and oxidative DNA damage, cells of all organisms have a complex network of repair systems that recognize, remove, and rebuild the injured sites. Damaged pyrimidines are generally removed by glycosylases that must scan the entire genome to locate lesions with sufficient fidelity to selectively remove the damage without inadvertent removal of normal bases. We report here studies conducted with a series of base analogs designed to test mechanisms of base recognition suggested by structural studies of glycosylase complexes. The oligonucleotide series examined here includes 5-halouracils with increasing substituent size and purine analogs placed opposite the target uracil with hydrogen, amino, and keto substituents in the 2- and 6-positions. The glycosylases studied here include Escherichia coli uracil-DNA glycosylase (UNG), E. coli mismatch uracil-DNA glycosylase (MUG), and the Methanobacterium thermoautotrophicum mismatch thymine-DNA glycosylase (TDG). The results of this study suggest that these glycosylases utilize several strategies for base identification, including (1) steric limitations on the size of the 5-substituent, (2) electronic-inductive properties of the 5-substituent, (3) reduced thermal stability of mispairs, and (4) specific functional groups on the purine base in the opposing strand. Contrary to predictions based upon the crystal structure, the preference of MUG for mispaired uracil over thymine is not based upon steric exclusion. Furthermore, the preference for mispaired uracil over uracil paired with adenine is more likely due to reduced thermal stability as opposed to specific recognition of the mispaired guanine. On the other hand, TDG, which exhibits modest discrimination among various pyrimidines, shows strong interactions with functional groups present on the purine opposite the target

pyrimidine. These results provide new insights into the mechanisms of base selection by DNA repair glycosylases.

L10 ANSWER 13 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2002:528599 Document No. 138:68793 Stimulation of Human Flap Endonuclease 1 by Human Immunodeficiency Virus Type 1 Integrase: Possible Role for Flap Endonuclease 1 in 5'-End Processing of Human Immunodeficiency Virus Type 1 Integration Intermediates. Faust, Emmanuel A.; Triller, Henry (SMBD-Jewish General Hospital, Lady Davis Institute for Medical Research, McGill University, McGill AIDS Center, Montreal, Can.). Journal of Biomedical Science (Basel, Switzerland), 9(3), 273-287 (English) 2002. CODEN: JBCIEA. ISSN: 1021-7770. Publisher: S. Karger AG.

AB Human immunodeficiency virus type 1 (HIV-1) DNA integration intermediates consist of viral and host DNA segments separated by a 5-nucleotide gap adjacent to a 5'-AC unpaired dinucleotide. These short-flap (pre-repair) integration intermediates are structurally similar to DNA loci undergoing long-patch base excision repair in mammalian cells. The cellular proteins flap endonuclease 1 (FEN-1), proliferating cell nuclear antigen, replication factor C, DNA ligase I and DNA polymerase δ are required for the repair of this type of DNA lesion. The role of FEN-1 in the base excision repair pathway is to cleave 5'-unpaired flaps in forked structures so that DNA ligase can seal the single-stranded breaks that remain following gap repair. The rate of excision by FEN-1 of 5'-flaps from short- and long-flap oligonucleotide substrates that mimic pre- and post-repair HIV-1 integration intermediates, resp., and the effect of HIV-1 integrase on these reactions were examined in the present study. Cleavage of 5'-flaps by FEN-1 in pre-repair HIV-1 integration intermediates was relatively inefficient and was further decreased 3-fold by HIV-1 integrase. The rate of removal of 5'-flaps by FEN-1 from post-repair HIV-1 integration intermediates containing relatively long (7-nucleotide) unpaired 5'-tails and short (1-nucleotide) gaps was increased 3-fold relative to that seen with pre-repair substrates and was further stimulated 5- to 10-fold by HIV-1 integrase. Overall, post-repair structures were cleaved 18 times more effectively in the presence of HIV-1 integrase than pre-repair structures. The site of cleavage was 1 or 2 nucleotides 3' of the branch point and was unaffected by HIV-1 integrase. Integrase alone had no detectable activity in removing 5'-flaps from either pre- or post-repair substrates.

L10 ANSWER 14 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2002:501714 Document No. 137:229744 Age-dependent decline of DNA repair activity for oxidative lesions in rat brain mitochondria. Chen, Dexi; Cao, Guodong; Hastings, Teresa; Feng, Yiqin; Pei, Wei; O'Horo, Cristine; Chen, Jun (Department of Neurology, Pittsburgh Institute for Neurodegenerative Disorders, University of Pittsburgh School of Medicine, Pittsburgh, PA, 15213, USA). Journal of Neurochemistry, 81(6), 1273-1284 (English) 2002. CODEN: JONRA9. ISSN: 0022-3042. Publisher: Blackwell Science Ltd..

AB Endogenous oxidative damage to brain mitochondrial DNA and mitochondrial dysfunction are contributing factors in aging and in the pathogenesis of a number of neurodegenerative diseases. Here, the authors characterized the regulation of base-excision-repair (BER) activity, the predominant repair mechanism for oxidative DNA lesions, in brain mitochondria as a function of age. Mitochondrial protein exts. were prepared from rat cerebral cortexes at the ages of embryonic day 17 (E17) or postnatal 1-, 2-, and 3-wk, or 5- and 30-mo. The total BER activity and the activity of essential BER enzymes were examined in mitochondria using in vitro DNA repair assay employing specific repair substrates. Mitochondrial BER activity showed marked age-dependent declines in the brain. The levels of overall BER activity were highest at E17, gradually decreased thereafter, and reached the lowest level at the age of 30-mo (.apprx.80% reduction). The decline of overall BER activity with age was attributed to the decreased expression of repair enzymes such as 8-oxoguanine-DNA glycosylase and DNA polymerase-γ, and consequently, the reduced activity at the steps of lesion-base incision, DNA repair synthesis, and DNA ligation in the BER pathway. These

results strongly suggest that the decline in BER activity may be an important mechanism contributing to the age-dependent accumulation of oxidative DNA lesions in brain mitochondria.

L10 ANSWER 15 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2002:233893 Document No. 137:90009 Substrate specificities and reaction mechanisms of mammalian base excision repair enzymes NTH1 and OGG1. Ide, Hiroshi (Department of Machematical and Life Sciences, Graduate School of Sciences, Hiroshima University, Higashi-Hiroshima, 739-8526, Japan). Kankyo Hen'igen Kenkyu, 23(3), 167-176 (Japanese) 2001. CODEN: KHKEEN. ISSN: 0910-0865. Publisher: Nippon Kankyo Hen'igen Gakkai.

AB A review. Reactive oxygen species generate structurally diverse base lesions in DNA. In E. coli cells, oxidative pyrimidine lesions are removed by Endo III and Endo VIII, whereas oxidative purine lesions by Fpg. In the present study, substrate specificities and reaction mechanisms of NTH1, a mammalian homolog of Endo III, and OGG1, a mammalian functional homolog of Fpg, were characterized using defined oligonucleotide substrates and the obtained results were compared to those of Endo III and Fpg. Mouse NTH1 (mNTH1) recognized not only urea (UR), thymine glycol (TG), 5,6-dihydrothymine (DHT), and 5-hydroxyuracil (HOU) derived from pyrimidine bases but also formamidopyrimidine (FAPY) derived from guanine. With both mNTH1 and human NTH1, the activity for FAPY was comparable to TG. Unlike Endo III, the activities of mNTH1 for these lesions were essentially independent of paired bases. Human OGG1 (hOGG1) recognized 7, 8dihydro-8-oxoguanine (OG) and FAPY. hOGG1 excised OG in a paired base-dependent manner but paired base effects were not evident for FAPY. The difference in the activity for the most preferred OG : C and the least preferred OG: A was 20-fold, while that for the most preferred FAPY: C and the least preferred FAPY : A was only 2.3-fold. These results indicate that FAPY : C is a good substrate for both NTH1 and OGG1, suggesting participation of the two enzymes in repair of this lesion in mammalian cells. In contrast, Endo III and Endo VIII recognized FAPY : C very poorly relative to TG. Determination of enzymic parameters revealed that catalytic rate consts. (kcat) of mNTH1 and hOGG1 were much lower than those of Endo III and Fpg. It seems that distinctive rate determining steps for the enzymic reaction are responsible for the differential paired base effects observed for Endo III and mNTH1. For Endo III with high kcat the rate determining step is flip out of a damaged base, thereby making the activity sensitive to paired bases. In contrast, for mNTH1 with low kcat the rate determining step is subsequent N-glycosylase and/or AP lyase, thereby making the activity insensitive to paired bases.

L10 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2001:911537 Document No. 136:207536 Review of progress in extreme ultraviolet lithography masks. Hector, Scott; Mangat, Pawitter (Motorola, Digital DNA Laboratories, Austin, TX, 78721, USA). Journal of Vacuum Science & Technology, B: Microelectronics and Nanometer Structures, 19(6), 2612-2616 (English) 2001. CODEN: JVTBD9. ISSN: 0734-211X. Publisher: American Institute of Physics.

AB A review. Extreme UV lithog. (EUVL) is a leading next generation lithog. technol. Significant progress has been made in developing mask fabrication processes for EUVL. The mask blank for EUVL consists of a low thermal expansion material substrate having a square photomask form factor that is coated with Mo/Si multilayers. SEMI stds. are being developed for mask substrates and mounting. Several com. suppliers are developing polishing processes for LTEM substrates, and they are progressing toward meeting the requirements for flatness, surface roughness, and defects defined in the a draft SEMI standard One of the challenges in implementing EUVL is to economically fabricate multilayer-coated mask blanks with no printable defects. Significant progress has been made in developing mask blank multilayer coating processes with low added defect d. Besides lowering the added defect d., methods to reduce defect printability, such as defect compensation and buffer layer smoothing, are being developed. Expts. indicate that Mo/Si multilayers that are deposited with ion

beam deposition tend to smooth substrate defects, and buffer layer films are being designed to enhance this effect. Targets for buffer layer smoothing are being defined using defect printability simulations. A method for using an electron beam to repair substrate defects after multilayer coating is also being investigated. The mask patterning process for EUVL is nearly the same as that for conventional binary optical lithog. masks. EUVL mask patterning efforts are focused on developing the EUV-specific aspects of the patterning process. Eight absorbers have been evaluated against the requirements for EUVL masks, and two absorbers appear most promising. Conventional membrane pellicles are not practical for EUVL, so thermophoretic protection is being developed. Expts. have indicated that thermophoretic protection is effective for >125 nm particles down to at least 50 mTorr pressure. A removable pellicle will be used to protect the mask from defects at all times except during wafer exposure.

L10 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2001:899868 Document No. 136:80786 Efficiency of Incision of an AP Site within Clustered DNA Damage by the Major Human AP Endonuclease.
David-Cordonnier, Marie-Helene; Cunniffe, Siobhan M. T.; Hickson, Ian D.; O'Neill, Peter (Medical Research Council Radiation and Genome Stability Unit, Harwell Didcot Oxon, OX11 0RD, UK). Biochemistry, 41(2), 634-642 (English) 2002. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.

AB A major DNA lesion induced by ionizing radiation and formed on removal of oxidized base lesions by various glycosylases is an apurinic/apyrimidinic site (AP site). The presence of an AP site within clustered DNA damage, induced following exposure to ionizing radiation or radiomimetic anticancer agents, may present a challenge to the repair machinery of the cell, if the major human AP endonuclease, HAP1, does not efficiently incise the AP site. In this study, specific oligonucleotide constructs containing an AP site located at several positions opposite to another damage [5,6-dihydrothymine (DHT), 8-oxoG, AP site, or various types of single strand breaks] on the complementary strand were used to determine the relative efficiency of the purified HAP1 protein in incising an AP site(s) from clustered DNA damage. A base damage (DHT and 8-oxoG) on the opposite strand has little or no influence on the rate of incision of an AP site by HAP1. In contrast, the presence of either a second AP site or various types of single strand breaks, when located one or three bases 3' to the base opposite to the AP site, has a strong inhibitory effect on the efficiency of incision of an AP site. The efficiency of binding of HAP1 to an AP site is reduced by .apprx.1 order of magnitude if a single strand break (SSB) is located one or three bases 3' to the site opposite to the AP site on the complementary strand. If the AP site and either a SSB or a second AP site are located at any of the other positions relative to each other, a double strand break may result.

L10 ANSWER 18 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2001:821865 Document No. 136:66114 Evidence of Powerful Substrate Electric Fields in DNA Photolyase: Implications for Thymidine Dimer Repair.
MacFarlane, Alexander W., IV; Stanley, Robert J. (Department of Chemistry, Temple University, Philadelphia, PA, 19122, USA). Biochemistry, 40(50), 15203-15214 (English) 2001. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.

AB DNA photolyase is a flavoprotein that repairs cyclobutylpyrimidine dimers by ultrafast photoinduced electron transfer. One unusual feature of this enzyme is the configuration of the FAD cofactor, where the isoalloxazine and adenine rings are nearly in van der Waals (vdW) contact. We have measured the steady-state and transient absorption spectra and excited-state decay kinetics of oxidized (FAD-containing, folate-depleted) Escherichia coli DNA photolyase with and without dinucleotide and polynucleotide single-stranded thymidine dimer substrates. The steady-state absorption spectrum for the enzyme-polynucleotide substrate complex showed a blue shift, as seen previously by Jorns et al. No shift was observed for the dinucleotide substrate, suggesting that there are significant differences in the binding geometry of dinucleotide vs. polynucleotide dimer lesions.

Evidence was obtained from transient absorption expts. for a long-lived charge-transfer complex involving the isoalloxazine of the FAD cofactor. No evidence of excited-state quenching was measurable upon binding either substrate. To explain these data, we hypothesize the existence of a large substrate elec. field in the cavity containing the FAD cofactor. A calcn. of the magnitude and direction of this dipolar elec. field is consistent with electrochromic band shifts for both S0 → S1 and S0 → S2 transitions. These observations suggest that the substrate dipolar elec. field may be a critical component in its electron-transfer-mediated repair by photolyase and that the unique relative orientation of the isoalloxazine and adenine rings may have resulted from the consequences of the dipolar substrate field.

L10 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2001:248226 Document No. 135:17778 Repair of double-strand breaks by homologous recombination in mismatch repair-defective mammalian cells. Elliott, Beth; Jasin, Maria (Cell Biology Program, Memorial Sloan-Kettering Cancer Center and Cornell University Graduate School of Medical Sciences, New York, NY, 10021, USA). Molecular and Cellular Biology, 21(8), 2671-2682 (English) 2001. CODEN: MCEBD4. ISSN: 0270-7306. Publisher: American Society for Microbiology.

AB Chromosomal double-strand breaks (DSBs) stimulate homologous recombination by several orders of magnitude in mammalian cells, including murine embryonic stem (ES) cells, but the efficiency of recombination decreases as the heterol. between the repair substrates increases. We have now examined homologous recombination in mismatch repair (MMR)-defective ES cells to investigate both the frequency of recombination and the outcome of events. Using cells with a targeted mutation in the msh2 gene, we found that the barrier to recombination between diverged substrates is relaxed for both gene targeting and intrachromosomal recombination. Thus, substrates with 1.5% divergence are 10-fold more likely to undergo DSB-promoted recombination in Msh2-/- cells than in wild-type cells. Although mutant cells can repair DSBs efficiently, examination of gene conversion tracts in recombinants demonstrates that they cannot efficiently correct mismatched heteroduplex DNA (hDNA) that is formed adjacent to the DSB. As a result, >20-fold more of the recombinants derived from mutant cells have uncorrected tracts compared with recombinants from wild-type cells. The results indicate that gene conversion repair of DSBs in mammalian cells frequently involves mismatch correction of hDNA rather than double-strand gap formation. In cells with MMR defects, therefore, aberrant recombinational repair may be an addnl. mechanism that contributes to genomic instability and possibly tumorigenesis.

L10 ANSWER 20 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2001:244446 Document No. 135:314338 Analysis of the binding of p53 to DNAs containing mismatched and bulged bases. Degtyareva, Natalya; Subramanian, Deepa; Griffith, Jack D. (Lineberger Comprehensive Cancer Center and the Department of Microbiology and Immunology, University of North Carolina, Chapel Hill, NC, 27599-7295, USA). Journal of Biological Chemistry, 276(12), 8778-8784 (English) 2001. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB The tumor suppressor protein p53 modulates cellular response to DNA damage by a variety of mechanisms that may include direct recognition of some forms of primary DNA damage. Linear 49-base pair duplex DNAs were constructed containing all possible single-base mismatches as well as a 3-cytosine bulge. Filter binding and gel retardation assays revealed that the affinity of p53 for a number of these lesions was equal to or greater than that of the human mismatch repair complex, hMSH2-hMSH6, under the same binding conditions. However, other mismatches including G/T, which is bound strongly by hMSH2-hMSH6, were poorly recognized by p53. The general order of affinity of p53 was greatest for a 3-cytosine bulge followed by A/G and C/C mismatches, then C/T and G/T mismatches, and finally all the other mismatches.

L10 ANSWER 21 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2001:93300 Document No. 135:252420 Homogeneous Preparations of 3'-Phosphoglycolate-Terminated Oligodeoxynucleotides from Bleomycin-Treated DNA as Verified by Electrospray Ionization Fourier Transform Ion Cyclotron Resonance Mass Spectrometry. Chen, Shuang; Hannis, James C.; Flora, Jason W.; Muddiman, David C.; Charles, Kwabena; Yu, Yin; Povirk, Lawrence F. (Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, VA, 23298, USA). Analytical Biochemistry, 289(2), 274-280 (English) 2001. CODEN: ANBCA2. ISSN: 0003-2697. Publisher: Academic Press.

AB Single- and double-strand breaks bearing 3'-phosphoglycolate termini are among the most frequent lesions formed in DNA by ionizing radiation and other oxidative mutagens. In order to obtain homogeneous prepns. of defined 3'-phosphoglycolate substrates for repair studies, 5'-32P-end-labeled partial duplex DNAs were treated with bleomycin, and individual cleavage products were isolated from polyacrylamide gels. The fragments were then treated with alkaline phosphatase and further purified by reverse-phase HPLC. Electrospray ionization Fourier transform ion cyclotron resonance (ESI-FTICR) mass spectrometry of the purified oligomers produced mol. ions of the expected masses, with no detectable contaminants. Gas-phase sequencing by tandem mass spectrometry of these single species yielded the expected sequence ions and confirmed the presence of phosphoglycolate on the 3'-terminal fragments only. The fragments could be relabeled with polynucleotide kinase to yield highly purified, high-specific-activity substrates for repair studies. (c) 2001 Academic Press.

L10 ANSWER 22 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2000:734171 Document No. 134:14673 Dinucleotide repeat expansion catalyzed by bacteriophage T4 DNA polymerase in vitro. Da Silva, Elizabeth Fidalgo; Reha-Krantz, Linda J. (Department of Biological Sciences, University of Alberta, Edmonton, AB, T6G 2E9, Can.). Journal of Biological Chemistry, 275(40), 31528-31535 (English) 2000. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB DNA replication normally occurs with high fidelity, but certain "slippery" regions of DNA with tracts of mono-, di-, and trinucleotide repeats are frequently mutation hot spots. We have developed an in vitro assay to study the mechanism of dinucleotide repeat expansion. The primer-template resembles a base excision repair substrate with a single nucleotide gap centered opposite a tract of nine CA repeats; nonrepeat sequences flank the dinucleotide repeats. DNA polymerases are expected to repair the gap, but further extension is possible if the DNA polymerase can displace the downstream oligonucleotide. We report here that the wild type bacteriophage T4 DNA polymerase carries out gap and strand displacement replication and also catalyzes a dinucleotide expansion reaction. Repeat expansion was not detected for an exonuclease-deficient T4 DNA polymerase or for Escherichia coli DNA polymerase I. The dinucleotide repeat expansion reaction catalyzed by wild type T4 DNA polymerase required a downstream oligonucleotide to "stall" replication and 3' → 5' exonuclease activity to remove the 3'-nonrepeat sequence adjacent to the repeat tract in the template strand. These results suggest that dinucleotide repeat expansion may be stimulated in vivo during DNA repair or during processing of Okazaki fragments.

L10 ANSWER 23 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2000:664911 Document No. 134:26869 Substrate specificity and reaction mechanism of murine 8-oxoguanine-DNA glycosylase. Zharkov, Dmitry O.; Rosenquist, Thomas A.; Gerchman, Sue Ellen; Grollman, Arthur P. (Laboratory of Chemical Biology, State University of New York at Stony Brook, Stony Brook, NY, 11794, USA). Journal of Biological Chemistry, 275(37), 28607-28617 (English) 2000. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB Genomic DNA is prone to oxidation by reactive oxygen species. A major product of DNA oxidation is the miscoding base 8-oxoguanine (8-oxoG). The mutagenic effects of 8-oxoG in mammalian cells are prevented by a DNA repair system consisting of

8-oxoguanine-DNA glycosylase (Ogg1), adenine-DNA glycosylase, and 8-oxo-dGTPase. We have cloned, overexpressed, and characterized mOgg1, the product of the murine ogg1 gene. MOgg1 is a DNA glycosylase/AP lyase belonging to the endonuclease III family of DNA repair enzymes. The AP lyase activity of mOgg1 is significantly lower than its glycosylase activity. MOgg1 releases 8-oxoG from DNA when paired with C, T, or G, but efficient DNA strand nicking is observed only with 8-oxoG:C. Binding of mOgg1 to oligonucleotides containing 8-oxoG:C is strong (KD = 51.5 nM), unlike other mispairs. The average residence time for mOgg1 bound to substrate containing 8-oxoG:C is 18.3 min; the time course for accumulation of the NaBH4-sensitive intermediate suggests a two-step reaction mechanism. Various analogs of 8-oxoG were tested as substrates for mOgg1. An electron-withdrawing or hydrogen bond acceptor moiety at C8 is required for efficient binding of mOgg1. A substituent at C6 and a keto group at C8 are required for cleavage. The proposed mechanism of 8-oxoG excision involves protonation of O8 or the deoxyribose oxygen moiety.

L10 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2000:488148 Document No. 133:330357 Possible involvement of a 72-kDa polypeptide in nucleotide excision repair of Chlorella pyrenoidosa identified by affinity adsorption and repair synthesis assay. Hsu, Todd; Sheu, Reou-Ching; Lai, Yi-Show (Institute of Marine Biotechnology, National Taiwan Ocean University, Chi-lung, 20224, Taiwan). Plant Science (Shannon, Ireland), 156(1), 95-102 (English) 2000. CODEN: PLSCE4. ISSN: 0168-9452. Publisher: Elsevier Science Ireland Ltd..

AB A DNA repair synthesis assay monitoring nucleotide excision repair (NER) was established in cell-free exts. of unicellular alga Chlorella pyrenoidosa using cisplatin- or mitomycin C-damaged plasmid DNA as the repair substrate. The algal exts. promoted a damage-dependent increase in 32P-dATP incorporation after normalization against an internal control. To identify the proteins responsible for NER, a biotin-labeled duplex 27 mer (2 μg) irradiated with or without UV (27 kJ m-2) was immobilized on streptavidin-conjugated agarose beads and incubated with C. pyrenoidosa exts. (50 μg) to pull down repair proteins. The exts. post incubation with beads carrying unirradiated 27 mer promoted an eightfold increase in repair synthesis in plasmid DNA (1 μg) damaged by 16.8 pmol of cisplatin. The exts. obtained after affinity adsorption with UV-damaged DNA ligand, however, failed to repair plasmid DNA treated with cisplatin, reflecting that some proteins crucial to NER had been sequestered by the damaged 27 mer. A polypeptide .apprx.70-72 kDa in mol. mass was found to bind much more strongly to the damaged DNA than to the control DNA after analyzing the proteins bound to the beads by SDS-PAGE, and this polypeptide is believed to play a role in NER in C. pyrenoidosa.

L10 ANSWER 25 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2000:482904 Document No. 133:116559 DNA repair enzyme MutY: Substrate recognition properties and kinetics of adenine glycosylase reaction. Porello, Silvia Laura (The Univ. of Utah, UT, USA). 142 pp. Avail. UMI, Order No. DA9947827 From: Diss. Abstr. Int., B 2000, 60(9), 4592 (English) 1999.

AB Unavailable

L10 ANSWER 26 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
2000:299002 Document No. 134:81340 Transcription-coupled and global genome repair in yeast and humans. Tijsterman, Marcel; Verhage, Richard A.; Brouwer, Jaap (Laboratory of Molecular Genetics, Leiden Institute of Chemistry, Gorlaeus Laboratories, Leiden University, Leiden, 2300 RA, Neth.). Frontiers in Molecular Biology, 22(DNA Recombination and Repair), 138-165 (English) 1999. CODEN: FMBIF5. Publisher: IRL Press at Oxford University Press.

AB A review, with 103 refs., on the processing or nucleotide excision repair substrates in vivo and genes specifically implicated in either of the two

subpathways, i.e., transcription coupled- and global genome repair. Since important insight into the complexity of nucleotide excision repair is provided by repair anal. of specific subfractions of the genome, there is first a discussion of the methodol. used to measure nucleotide excision repair inside living cells.

L10 ANSWER 27 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
1999:388932 Document No. 131:196229 Substrate Specificity of Deinococcus radiodurans Fpg Protein. Sentuerker, Sema; Bauche, Cecile; Laval, Jacques; Dizdaroglu, Miral (Chemical Science and Technology Laboratory, National Institute of Standards and Technology, Gaithersburg, MD, 20899-8311, USA). Biochemistry, 38(29), 9435-9439 (English) 1999. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.

AB A DNA repair enzyme has recently been isolated from the ionizing radiation-resistant bacterium Deinococcus radiodurans [Bauche, C., and Laval, J. (1999) J. Bacteriol. 181, 262-269]. This enzyme is a homolog of the Fpg protein of Escherichia coli. We investigated the substrate specificity of this enzyme for products of oxidative DNA base damage using gas chromatog./isotope-dilution mass spectrometry and DNA substrates, which were either γ-irradiated or treated with H2O2/Fe(III)-EDTA/ascorbic acid. Excision of purine lesions 2,6-diamino-4-hydroxy-5- formamidopyrimidine (FapyGua), 4,6-diamino-5-formamidopyrimidine (FapyAde), and 8-hydroxyguanine (8-OH-Gua) was observed among 17 lesions detected in damaged DNA substrates. The extent of excision was determined as a function of enzyme concentration, time, and substrate concentration FapyGua and FapyAde were excised with similar specificities from three DNA substrates, whereas 8-OH-Gua was the least preferred lesion. The results show that D. radiodurans Fpg protein and its homolog E. coli Fpg protein excise the same modified DNA bases, but the excision rates of these enzymes are significantly different. Formamidopyrimidines are preferred substrates of D. radiodurans Fpg protein over 8-OH-Gua, whereas E. coli Fpg protein excises these three lesions with similar efficiencies from various DNA substrates. Substrate specificities of these enzymes were also compared with that of Saccharomyces cerevisiae Ogg1 protein, which excises FapyGua and 8-OH-Gua, but not FapyAde.

L10 ANSWER 28 OF 42 CAPLUS COPYRIGHT 2005 ACS on STN
1998:704557 Document No. 130:61943 Stereoselectivity of human nucleotide excision repair promoted by defective hybridization. Hess, Martin T.; Naegeli, Hanspeter; Capobianco, Massimo (Institute of Pharmacology and Toxicology, University of Zurich-Tierspital, Zurich, CH-8057, Switz.). Journal of Biological Chemistry, 273(43), 27867-27872 (English) 1998. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB To assess helical parameters that dictate fast or slow removal of carcinogen-DNA adducts, we probed human nucleotide excision repair (NER) activity with DNA containing L-deoxyriboses. Unlike natural lesions such as pyrimidine dimers or base adducts, L-deoxyribonucleosides (the mirror images of normal D-deoxyribonucleosides) involve neither the addition nor the loss of covalent bonds or functional groups and hence exclude modulation of repair efficiency by adduct chemical and size. Previous studies showed that single L-deoxyribonucleosides distort DNA backbones but are accommodated in the double helix with intact hydrogen bonding between complementary strands. Here, we found that such single L-enantiomers are rejected as excision repair substrates in a NER-proficient cell extract However, the same L-deoxyribose moiety stimulates NER activity upon incorporation into a nonhybridizing site of one or, more effectively, two base mismatches. In contrast to single L-deoxyriboses, multiple consecutive L-deoxyriboses interfere with normal hybridization; in this case, the intrinsic derangement of base pairing was sufficient to promote the excision of a cluster of three adjacent L-deoxyribonucleosides without any requirement for mismatches. Thus, using stereoselective substrates, we demonstrate the participation of a recognition subunit that guides human NER activity to sites of defective Watson-

Crick strand pairing. This conformational sensor detects labile hydrogen bonds irresp. of the type of deoxyribonucleotide modification.

=> D L13 2,4,6,11,15,19,23,24,29 CBIB ABS

L13 ANSWER 2 OF 49 CAPLUS COPYRIGHT 2005 ACS on STN
2005:59452 Document No. 142:290517 Editorial - zinc finger nuclease-boosted gene targeting: Toward clinical gene repair/alteration and custom site-specific integrative gene therapy. Bertolotti, Roger (CNRS, Gene Therapy and Regulation Research, Faculty of Medicine, University of Nice Sophia, Nice, 06107, Fr.). Gene Therapy and Regulation, 2(3), 177-189 (English) 2004. CODEN: GTREBR. ISSN: 1388-9532. Publisher: Brill Academic Publishers.
AB A review on gene repair/alteration and targeted integration of therapeutic transgenes, chimeric Zn-finger nucleases as basic gene targeting boosters, and clin. gene targeting.

L13 ANSWER 4 OF 49 CAPLUS COPYRIGHT 2005 ACS on STN
2004:624941 Document No. 142:275776 Engineering and applications of chimeric nucleases. Kandavelou, K.; Mani, M.; Durai, S.; Chandrasegaran, S. (Department of Environmental Health Sciences, Bloomberg School of Public Health, The Johns Hopkins University, Baltimore, MD, 21205-2179, USA). Nucleic Acids and Molecular Biology, 14(Restriction Endonucleases), 413-434 (English) 2004. CODEN: NAMBE8. ISSN: 0933-1891. Publisher: Springer-Verlag.
AB A review discusses the progress towards targeted correction of a genetic defect. This involves two steps: engineering of chimeric nucleases, the mol. tools necessary to make a chromosomal double strand break at a chosen site within the human genome; and application of these mol. tools for targeted chromosomal cleavage and correction of a genetic defect by inducing homologous recombination at that locus in cells.

L13 ANSWER 6 OF 49 CAPLUS COPYRIGHT 2005 ACS on STN
2004:371049 Document No. 140:369922 Construction and use of chimeric nucleases to stimulate gene targeting for gene therapy. Baltimore, David; Porteus, Matthew (California Institute of Technology, USA). PCT Int. Appl. WO 2004037977 A2 20040506, 85 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US27958 20030905. PRIORITY: US 2002-PV408454 20020905; US 2002-PV419341 20021017; US 2003-PV484788 20030703.
AB Gene targeting is a technique to introduce genetic change into one or more specific locations in the genome of a cell. For example, gene targeting can introduce genetic change by modifying, repairing, attenuating or inactivating a target gene or other chromosomal DNA. In one aspect, this disclosure relates to methods and compns. for gene targeting with high efficiency in a cell. This disclosure also relates to methods of treating or preventing a genetic disease in an individual in need thereof. Further disclosed are chimeric nucleases and vectors encoding chimeric nucleases. The system used to study gene targeting was based on the correction of a mutated green fluorescent protein (GFP) gene. Three different chimeric nucleases were designed, each driven by the CMV promoter and containing a nuclear localization signal, a DNA-binding domain comprising zinc finger(s), and a cleavage domain. Gene targeting of GFP using GFP specific nucleases and gene targeting of the human CD8 gene using chimeric nucleases is described.

L13 ANSWER 11 OF 49 CAPLUS COPYRIGHT 2005 ACS on STN
2003:448503 Document No. 139:31459 Chimeric nucleases stimulate gene targeting in human cells. Porteuus, Matthew H.; Baltimore, David (Dep. Biology, California Inst. Technology, Pasadena, CA, 91125, USA). Science (Washington, DC, United States), 300(5620), 763 (English) 2003. CODEN: SCIEAS. ISSN: 0036-8075. Publisher: American Association for the Advancement of Science.

AB Chimeric nucleases (CN) containing zinc finger DNA-binding domains were modified and tested for stimulation of gene targeting in human 293 cells. Effects of binding site spacing and size of linker region (between endonuclease domain and zinc finger) on gene targeting stimulation were examined Gene targeting at homodimer and heterodimer binding sites were compared.

L13 ANSWER 15 OF 49 CAPLUS COPYRIGHT 2005 ACS on STN
2002:637874 Document No. 137:180745 Nucleotide polymorphism detection with chimeric oligonucleotide primers and nuclease cleavage.
Sagawa, Hiroaki; Kobayashi, Eiji; Kato, Ikunoshin (Takara Shuzo Co., Ltd., Japan). PCT Int. Appl. WO 2002064833 A1 20020822, 77 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2002-JP1222 20020214. PRIORITY: JP 2001-39268 20010215; JP 2001-40721 20010216; JP 2001-101055 20010330; JP 2001-177381 20010612; JP 2001-290384 20010925; JP 2001-338440 20011102; JP 2001-368929 20011203.

AB Chimeric oligonucleotide primers useful in detecting nucleotide polymorphisms, comprising deoxyribonucleotides and ribonucleotides where 3' end is modified to prevent extension by DNA polymerase, are disclosed. In the presence of a mismatch, the chimeric oligonucleotide is not cleaved by a nuclease, whereas in the absence of a mismatch, it is cleaved by a nuclease, creating a new 3'-terminal for extension by DNA polymerase. Either RNase H or restriction enzymes are used. The chimeric oligonucleotide is labeled with a fluorescent substance, and possibly with a quenching substance, so that its cleavage could by detected by fluorescence polarization. Nucleotide analogs such as deoxyriboinosine nucleotides, deoxyribouracil nucleotides, or (α-S) ribonucleotides, having modification at the 3'-OH group of the ribose, are preferably used. Use of the oligonucleotides for genotyping anal. and a kit therefor are claimed. Chimeric oligonucleotide having the 3'-OH group of the nucleotide at 3'-end protected with aminohexyl group and their use in detecting the single nucleotide polymorphisms in human c-Ki-ras gene, or human CYP2C19 gene, combined with RNase HII, are described.

L13 ANSWER 19 OF 49 CAPLUS COPYRIGHT 2005 ACS on STN
2001:684612 Document No. 136:243633 Studies on zinc finger chimeric nucleases to refine and improve them for in vivo applications.
Smith, James Jefferson (Johns Hopkins Univ., Baltimore, MD, USA). 195 pp. Avail. UMI, Order No. DA9993189 From: Diss. Abstr. Int., B 2001, 61(10), 5198 (English) 2001.

AB Unavailable

L13 ANSWER 23 OF 49 CAPLUS COPYRIGHT 2005 ACS on STN
2001:9001 Document No. 135:72070 Stimulation of homologous recombination through targeted cleavage by chimeric nucleases.
Bibikova, Marina; Carroll, Dana; Segal, David J.; Trautman, Jonathan K.;

Smith, Jeff; Kim, Yang-Gyun; Chandrasegaran, Srinivasan (Department of Biochemistry, University of Utah School of Medicine, Salt Lake City, UT, 84132, USA). Molecular and Cellular Biology, 21(1), 289-297 (English) 2001. CODEN: MCEBD4. ISSN: 0270-7306. Publisher: American Society for Microbiology.

AB Chimeric nucleases that are hybrids between a nonspecific DNA cleavage domain and a zinc finger DNA recognition domain were tested for their ability to find and cleave their target sites in living cells. Both engineered DNA substrates and the nucleases were injected into Xenopus laevis oocyte nuclei, in which DNA cleavage and subsequent homologous recombination were observed Specific cleavage required two inverted copies of the zinc finger recognition site in close proximity, reflecting the need for dimerization of the cleavage domain. Cleaved DNA mols. were activated for homologous recombination; in optimum conditions, essentially 100% of the substrate recombined, even though the DNA was assembled into chromatin. The original nuclease has an 18-amino-acid linker between the zinc finger and cleavage domains, and this enzyme cleaved in oocytes at paired sites separated by spacers in the range of 6 to 18 bp, with a rather sharp optimum at 8 bp. By shortening the linker, the range of effective site sepns. could be narrowed significantly. With no intentional linker between the binding and cleavage domains, only binding sites exactly 6 bp apart supported efficient cleavage in oocytes. Also, two chimeric enzymes with different binding specificities could collaborate to stimulate recombination when their individual sites were appropriately placed. Because the recognition specificity of zinc fingers can be altered exptl., this approach holds great promise for inducing targeted recombination in a variety of organisms.

L13 ANSWER 24 OF 49 CAPLUS COPYRIGHT 2005 ACS on STN

2000:680449 Document No. 134:14615 Requirements for double-strand cleavage by chimeric restriction enzymes with zinc finger DNA-recognition domains. Smith, Jeff; Bibikova, Marina; Whitby, Frank G.; Reddy, A. R.; Chandrasegaran, Srinivasan; Carroll, Dana (Department of Environmental Health Sciences, The Johns Hopkins University School of Hygiene and Public Health, Baltimore, MD, 21205, USA). Nucleic Acids Research, 28(17), 3361-3369 (English) 2000. CODEN: NARHAD. ISSN: 0305-1048. Publisher: Oxford University Press.

AB This study concerns chimeric restriction enzymes that are hybrids between a zinc finger DNA-binding domain and the non-specific DNA-cleavage domain from the natural restriction enzyme FokI. Because of the flexibility of DNA recognition by zinc fingers, these enzymes are potential tools for cleaving DNA at arbitrarily selected sequences. Efficient double-strand cleavage by the chimeric nucleases requires two binding sites in close proximity. When cuts were mapped on the DNA strands, it was found that they occur in pairs separated by -4 bp with a 5' overhang, as for native FokI. Furthermore, amino acid changes in the dimer interface of the cleavage domain abolished activity. These results reflect a requirement for dimerization of the cleavage domain. The dependence of cleavage efficiency on the distance between two inverted binding sites was determined and both upper and lower limits were defined. Two different zinc finger combinations binding to non-identical sites also supported specific cleavage. Mol. modeling was employed to gain insight into the precise location of the cut sites. These results define requirements for effective targets of chimeric nucleases and will guide the design of novel specificities for directed DNA cleavage in vitro and in vivo.

L13 ANSWER 29 OF 49 CAPLUS COPYRIGHT 2005 ACS on STN

1999:566699 Document No. 131:209652 Chimeric restriction enzymes. What is next?. Chandrasegaran, Srinivasan; Smith, Jeff (Dep. Environmental Health Sciences, School Public Health, Johns Hopkins Univ., Baltimore, MD, 21205, USA). Biological Chemistry, 380(7/8), 841-848 (English) 1999. CODEN: BICHF3. ISSN: 1431-6730. Publisher: Walter de Gruyter & Co..

AB A review is given with many refs. Chimeric restriction enzymes are a novel class of engineered nucleases in which the non-specific DNA cleavage domain of FokI (a

type IIS restriction endonuclease) is fused to other DNA-binding motifs. The latter include the 3 common eukaryotic DNA-binding motifs, namely the helix-turn-helix motif, the Zn finger motif and the basic helix-loop-helix protein containing a Leu zipper motif. Such chimeric nucleases were shown to make specific cuts in vitro very close to the expected recognition sequences. The most important chimeric nucleases are those based on Zn finger DNA-binding proteins because of their modular structure. Recently, 1 such chimeric nuclease, Zif-QQR-FN was shown to find and cleave its target in vivo. This was tested by microinjection of DNA substrates and the enzyme into frog oocytes. The injected enzyme made site-specific double-strand breaks in the targets even after assembly of the DNA into chromatin. This cleavage activated the target mols. for efficient homologous recombination. Since the recognition specificity of Zn fingers can be manipulated exptl., chimeric nucleases could be engineered so as to target a specific site within a genome. The availability of such engineered chimeric restriction enzymes should make it feasible to do genome engineering, also commonly referred to as gene therapy.

```
=> E BALTIMORE D/AU
=> S E3,E4
             36 "BALTIMORE D"/AU
            567 "BALTIMORE DAVID"/AU
L14         603 ("BALTIMORE D"/AU OR "BALTIMORE DAVID"/AU)

=> E PORTEUS M/AU
=> S E4,E5
              1 "PORTEUS MATTHEW"/AU
             11 "PORTEUS MATTHEW H"/AU
L15          12 ("PORTEUS MATTHEW"/AU OR "PORTEUS MATTHEW H"/AU)

=> S L14,L15
L16         613 (L14 OR L15)

=> S L16 AND L6
L17           2 L16 AND L6

=> S L16 AND L10
L18           0 L16 AND L10

=> D L17 1-2 CBIB AB

L17  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2005 ACS on STN
2004:371049   Document No. 140:369922  Construction and use of chimeric
nucleases to stimulate gene targeting for gene therapy.
Baltimore, David; Porteus, Matthew (California Institute
of Technology, USA).  PCT Int. Appl. WO 2004037977 A2 20040506, 85 pp.
DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ,
CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL,
PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG,
US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM,
CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT,
SE, SN, TD, TG, TR.  (English).  CODEN: PIXXD2.  APPLICATION: WO
2003-US27958 20030905.  PRIORITY: US 2002-PV408454 20020905; US
2002-PV419341 20021017; US 2003-PV484788 20030703.
AB  Gene targeting is a technique to introduce genetic change into one or more
    specific locations in the genome of a cell.  For example, gene targeting can
    introduce genetic change by modifying, repairing, attenuating or inactivating a
    target gene or other chromosomal DNA.  In one aspect, this disclosure relates to
    methods and compns. for gene targeting with high efficiency in a cell.  This
```

disclosure also relates to methods of treating or preventing a genetic disease in an individual in need thereof. Further disclosed are chimeric nucleases and vectors encoding chimeric nucleases. The system used to study gene targeting was based on the correction of a mutated green fluorescent protein (GFP) gene. Three different chimeric nucleases were designed, each driven by the CMV promoter and containing a nuclear localization signal, a DNA-binding domain comprising zinc finger(s), and a cleavage domain. Gene targeting of GFP using GFP specific nucleases and gene targeting of the human CD8 gene using chimeric nucleases is described.

L17 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
2003:448503 Document No. 139:31459 Chimeric nucleases stimulate gene targeting in human cells. Porteuus, Matthew H.; Baltimore, David (Dep. Biology, California Inst. Technology, Pasadena, CA, 91125, USA). Science (Washington, DC, United States), 300(5620), 763 (English) 2003. CODEN: SCIEAS. ISSN: 0036-8075. Publisher: American Association for the Advancement of Science.

AB Chimeric nucleases (CN) containing zinc finger DNA-binding domains were modified and tested for stimulation of gene targeting in human 293 cells. Effects of binding site spacing and size of linker region (between endonuclease domain and zinc finger) on gene targeting stimulation were examined Gene targeting at homodimer and heterodimer binding sites were compared.

```
FILE 'REGISTRY' ENTERED AT 14:03:22 ON 12 MAY 2005

=> S NUCLEASE/CN;S ENDONUCLEASE/CN
L1             1 NUCLEASE/CN


L2             1 ENDONUCLEASE/CN

FILE 'CAPLUS' ENTERED AT 14:03:44 ON 12 MAY 2005

=> S CHIMERIC;S L3(3A)(L1,L2)
          43553 CHIMERIC
             29 CHIMERICS
L3        43564 CHIMERIC
                (CHIMERIC OR CHIMERICS)


           2517 L1
           1516 L2
L4           10 L3(3A)((L1 OR L2))

=> S NUCLEASE
          20347 NUCLEASE
           6185 NUCLEASES
L5        24458 NUCLEASE
                (NUCLEASE OR NUCLEASES)

=> S ENDONUCLEASE
          26418 ENDONUCLEASE
           7957 ENDONUCLEASES
L6        30697 ENDONUCLEASE
                (ENDONUCLEASE OR ENDONUCLEASES)

=> S L3(3A)(L1,L2,L5,L6)
           2517 L1
           1516 L2
L7           80 L3(3A)((L1 OR L2 OR L5 OR L6))

=> S REPAIR
          74292 REPAIR
           3240 REPAIRS
L8        76123 REPAIR
                (REPAIR OR REPAIRS)

=> S L7 AND L8
L9             9 L7 AND L8

=> D 1-9 CBIB ABS

L9   ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2005 ACS on STN
2005:59452  Document No. 142:290517  Editorial - zinc finger nuclease-boosted
     gene targeting: Toward clinical gene repair/alteration and
     custom site-specific integrative gene therapy.  Bertolotti, Roger (CNRS,
     Gene Therapy and Regulation Research, Faculty of Medicine, University of
     Nice Sophia, Nice, 06107, Fr.).  Gene Therapy and Regulation, 2(3),
     177-189 (English) 2004.  CODEN: GTREBR.  ISSN: 1388-9532.  Publisher:
     Brill Academic Publishers.
AB   A review on gene repair/alteration and targeted integration of therapeutic
     transgenes, chimeric Zn-finger nucleases as basic gene targeting boosters, and
     clin. gene targeting.


L9   ANSWER 2 OF 9  CAPLUS  COPYRIGHT 2005 ACS on STN
```

2004:902401 Document No. 141:374706 Chimeric polypeptides comprising DNA modifying activity and use in cell-cycle regulation and tumor therapy. Kuehne, Christian; Simoncsits, Andras (International Centre for Genetic Engineering and Biotechnology, Italy). PCT Int. Appl. WO 2004092194 A2 20041028, 69 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-EP4062 20040416. PRIORITY: IT 2003-MI821 20030418.

AB The present invention concerns chimeric proteins that contain a polypeptidic region, consisting of a specific affinity for the binding to specific DNA sequences, or a polypeptidic region consisting of a DNA modifying activity, and this chimeric protein is capable to cross biol. membranes due to the presence of a region that contains delivery activity. The invention also relates the isolated polynucleotides that code for the chimeric mols. of the invention. In another embodiment, based on the activities of the polypeptides of the invention to interfere with key points of the cell-cycle regulation and the cellular checkpoints due to their introduction of DNA double strand breaks, the invention contains various procedures that are characterized by the use of said polypeptides for cells in vivo and provides an activity for the modification of specific sites of the DNA contained in a cell. The invention also contains procedures that use the chimeric mols. of the invention to screen for new delivery activities or combinations of delivery activities. The invention further provides for the therapeutic use of said compns. as anti-proliferative, anti-neoplastic, antibiotic, antiparasitic or antiviral agents.

L9 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

2004:686205 Document No. 141:235452 Zinc finger nuclease-boosted gene targeting and synergistic transient regenerative gene therapy for long-term stem cell gene therapy. Bertolotti, Roger (CNRS, Gene Therapy and Regulation Research, Faculty of Medicine, University of Nice Sophia Antipolis, Nice, 06107, Fr.). Biogenic Amines, 18(3-6), 503-538 (English) 2004. CODEN: BIAME7. ISSN: 0168-8561. Publisher: VSP BV.

AB A review. Stem cells have both self-renewing and homing/differentiative capabilities and thereby provide for life-long cell replacement in tissues and organs. They are therefore the ideal targets for most gene therapy protocols, i.e. both for long-term and transient gene expression protocols where they are either the long term carriers of the therapeutic gene (inherited/degenerative disease) or the mobilized/recruited targets of a transient regenerative process such as the formation of new blood vessels. Long-term gene therapy is thus amenable to synergistic combinations where ex vivo/in vivo genetic engineering of stem cells can be associated with in vivo transient topical expression of minigenes encoding various factors such as homing, regenerative and differentiative ones. Such a strategy is still hampered by many hurdles of which random integration of therapeutic DNA is a major safety concern. Emerging technologies are however aimed at efficient site-specific integration of therapeutic transgenes and at endogenous gene repair/modification. Promising site-specific integration vectors are at the pre-clin. stage and rely on an adeno-associated virus (AAV) rep platform or on phage phiC31 integrase. However, unlike these approaches, gene targeting is driven by homologous recombination and has thus target flexibility. It mediates DNA exchanges between chromosomal DNA and transfecting/transducing DNA, thereby providing the means to modify at will the sequence of target chromosomal DNA. Gene targeting stands thus as the ultimate process both for gene repair/alteration and targeted (i.e. site-specific) transgene integration. Such a process is however highly inefficient unless target chromosomal DNA is struck by a double-strand break (DSB). In addition, it is overwhelmed by random integration. To increase gene targeting

frequency and eliminate random integration, the authors devised an approach that relies on the transfer into target cells of premade presynaptic filaments, i.e. the very stoichiometric complexes between recombinase protein and single-stranded DNA (ssDNA) that mediate the key reaction from homologous recombination (homologous DNA pairing-strand exchange with double-stranded [ds] DNA). Upon publication of the enzymic properties of recombinase RAD51, the authors invented chimeric presynaptic filaments with a dsDNA core, and shifted from gene conversion to 'true' gene targeting. Chimeric zinc finger nucleases are now available that create sequence-specific DSBs in target chromosomal DNA and stimulate gene targeting as expected. Such designed nucleases open exciting potentialities for standard gene targeting (non-viral) but also for emerging AAV gene targeting that has been shown to be boosted by DSB too. In these approaches, gene targeting frequency is raised to the random-integration level, i.e. .apprx.1% of transfected/transduced cells. The authors current approach is thus discussed in terms of synergistic combinations in which random-integration is blocked by the use of premade presynaptic complexes while homologous recombination is promoted both by premade presynaptic complexes and by sequence-specific DSB of target chromosomal DNA. Long-term gene therapy is thus amenable to sophisticated protocols in which stem-cell gene-targeting is combined with transient regenerative gene therapy, and might therefore apply to the treatment of the neurol. symptoms of the Lesch-Nyhan disease in which the target is the authors paragon model, the hypoxanthine-guanine phosphoribosyl transferase (HPRT) gene.

L9 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
2004:371049 Document No. 140:369922 Construction and use of chimeric nucleases to stimulate gene targeting for gene therapy.
Baltimore, David; Porteus, Matthew (California Institute of Technology, USA). PCT Int. Appl. WO 2004037977 A2 20040506, 85 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US27958 20030905. PRIORITY: US 2002-PV408454 20020905; US 2002-PV419341 20021017; US 2003-PV484788 20030703.

AB Gene targeting is a technique to introduce genetic change into one or more specific locations in the genome of a cell. For example, gene targeting can introduce genetic change by modifying, repairing, attenuating or inactivating a target gene or other chromosomal DNA. In one aspect, this disclosure relates to methods and compns. for gene targeting with high efficiency in a cell. This disclosure also relates to methods of treating or preventing a genetic disease in an individual in need thereof. Further disclosed are chimeric nucleases and vectors encoding chimeric nucleases. The system used to study gene targeting was based on the correction of a mutated green fluorescent protein (GFP) gene. Three different chimeric nucleases were designed, each driven by the CMV promoter and containing a nuclear localization signal, a DNA-binding domain comprising zinc finger(s), and a cleavage domain. Gene targeting of GFP using GFP specific nucleases and gene targeting of the human CD8 gene using chimeric nucleases is described.

L9 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
2001:731046 Document No. 135:283927 Chimeric proteins for detection and quantitation of DNA mutations, DNA sequence variations, DNA damage and DNA mismatches. McCutchen-Maloney, Sandra L. (Regents of the University of California, USA). PCT Int. Appl. WO 2001073079 A2 20011004, 128 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,

HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US9700 20010326. PRIORITY: US 2000-PV192764 20000328; US 2000-650855 20000829.

AB Chimeric proteins having both DNA mutation regions binding activity and nuclease activity are synthesized by recombinant technol. The proteins are of the general formula A-L-B and B-L-A where A is a peptide having DNA mutation region binding activity, L is a linker and B is a peptide having nuclease activity. The chimeric proteins are useful for detection and identification of DNA sequence variations including DNA mutations (including DNA damage and mismatches) by binding to the DNA mutation and cutting the DNA once the DNA mutation is detected. Preparation of chimeric encoding cDNA by PCR, recombinant preparation of 12 chimeric proteins such as Nuc-Linker-XPA fragment, and assaying for activity for DNA damage detection were also described. The method may be used for disease detection.

L9 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

2000:774072 Document No. 133:331776 Determining analyte mobility using laser-inducible labels and low-intensity laser. Houtsmuller, Adriaan Barend; Vermeulen, Willem (Erasmus Universiteit Rotterdam, Neth.). Eur. Pat. Appl. EP 1048952 A1 20001102, 17 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 1999-201361 19990429.

AB The invention relates to the field of measuring or determining mobilities of analytes or mol. (complexes). The invention provides a method for determining the mobility of a certain analyte in a set volume comprising labeling said analyte with a laser-inducible moiety and subjecting a spot or area in a pre-determined plane through said set volume to a focused laser beam of relatively low intensity for a relatively long time thereby inducing a measurable change in said moiety when exposed to said laser beam and determining the distribution of laser-exposed moiety in said plane. To study the nuclear organization and dynamics of nucleotide excision repair, the endonuclease ERCC1 was tagged with green fluorescent protein and its mobility was monitored in CHO cells. The tagged ERCC1 complexed with XPF. In the absence of DNA damage, the complex moved freely through the nucleus with a diffusion coefficient consistent with its size. UV light-induced DNA damage caused a transient dose-dependent immobilization of the complex. After four minutes, the complex regained mobility.

L9 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

2000:553718 Document No. 133:160582 Gene repair involving homologous recombination induced by in vivo double-stranded cleavage of targeting DNA mediated by chimeric restriction endonuclease. Choulika, Andre; Mulligan, Richard C. (Children's Medical Center Corporation, USA; Institute Pasteur). PCT Int. Appl. WO 2000046386 A2 20000810, 38 pp. DESIGNATED STATES: W: AU, CA, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US3014 20000203. PRIORITY: US 1999-PV118669 19990203.

AB Methods of modifying, repairing, attenuating and inactivating a gene or other chromosomal DNA in a cell through chimeric restriction endonuclease (or meganuclease)-induced homologous recombination are disclosed. 101The method is exemplified by introducing into a cell a vector containing a targeting DNA homologous to a chromosomal target sites and is flanked by specific sites for restriction endonuclease I-SceI (a Saccharomyces cerevisiae intron-encoded rare-cutter endonuclease recognizing 18-bp sequence) or meganuclease, and cDNA encoding I-SceI or meganuclease. The I-SceI site is recognized and cleaved in vivo to relase the repair matrix and induce homologous recombination. The method

has applications in treating or prophylaxis of a genetic disease in an individual in need.

L9 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
1999:182359 Document No. 131:69809 Targeted Linearization of DNA in Vivo. Liang, Chien-Ping; Garrard, William T. (Department of Molecular Biology and Oncology, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, 75235-9140, USA). Methods (Orlando, Florida), 17(2), 95-103 (English) 1999. CODEN: MTHDE9. ISSN: 1046-2023. Publisher: Academic Press.

AB In the past decade, site-specific chromosomal DNA cleavage mediated by DNA endonucleases has been used to examine diverse aspects of chromosome structure and function in eukaryotes, such as DNA topol., replication, transcription, recombination, and repair. Here we describe a method with which chromosomes can be linearized at any predefined position in vivo. Yeast homothallic switching endonuclease (HO endo), a sequence-specific double-strand nuclease involved in mating-type switching, is employed for targeting DNA cleavage. HO endo contains discrete functional domains: a N-terminal nuclease and a C-terminal DNA-binding domain, thereby allowing construction of a chimeric nuclease with the cutting site distinct from the original HO recognition sequence. The expression of the nuclease is engineered to be controlled by a tightly regulated, inducible promoter. The cut sites recognized by HO endo or its derivs. are introduced specifically at desired positions in the yeast genome by homologous recombination. Here we present exptl. procedures and review some applications based on this approach in yeast and other biol. systems. (c) 1999 Academic Press.

L9 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
1998:45423 Document No. 128:200619 Creation of a fully functional human chimeric DNA repair protein. Combining O6-methylguanine DNA methyltransferase (MGMT) and AP endonuclease (APE/redox effector factor 1 (Ref 1)) DNA repair proteins. Hansen, Warren K.; Deutsch, Walter A.; Yacoub, Adley; Xu, Yi; Williams, David A.; Kelley, Mark R. (Dep. Pediatrics, Pennington Biomed. Res. Cent., Baton Rouge, LA, 70808, USA). Journal of Biological Chemistry, 273(2), 756-762 (English) 1998. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB A dose-limiting toxicity of certain chemotherapeutic alkylating agents is their toxic effects on nontarget tissues such as the bone marrow. To overcome the myelosuppression observed by chemotherapeutic alkylating agents, one approach is to increase the level of DNA repair proteins in hematopoietic stem and progenitor cells. Toward this goal, we have constructed a human fusion protein consisting of O6-methylguanine DNA methyltransferase coupled with an apurinic endonuclease, resulting in a fully functional protein for both O6-methylguanine and apurinic/apyrimidinic (AP) site repair as determined by biochem. anal. The chimeric protein protected AP endonuclease -deficient Escherichia coli cells against Me methanesulfonate and hydrogen peroxide (H2O2) damage. A retroviral construct expressing the chimeric protein also protected HeLa cells against 1,3-bis(2-chloroethyl)-1- nitrosourea and Me methanesulfonate cytotoxicity either when these agents were used sep. or in combination. Moreover, as predicted from previous anal., truncating the amino 150 amino acids of the apurinic endonuclease portion of the O6-methylguanine DNA methyltransferase-apurinic endonuclease protein resulted in the retention of O6-methylguanine DNA methyltransferase activity but loss of all AP endonuclease activity. These results demonstrate that the fusion of O6-methylguanine DNA methyltransferase and apurinic endonuclease proteins into a combined single repair protein can result in a fully functional protein retaining the repair activities of the individual repair proteins. These and other related constructs may be useful for protection of sensitive tissues and, therefore, are candidate constructs to be tested in preclin. models of chemotherapy toxicity.

	L #	Hits	Search Text	DBs
1	L1	42156	chimeric	US-PGPUB; USPAT
2	L2	48358	nuclease or endonuclease	US-PGPUB; USPAT
3	L3	168368	repair	US-PGPUB; USPAT
4	L4	2109	L1 SAME L2	US-PGPUB; USPAT
5	L5	463	L4 AND L3	US-PGPUB; USPAT
6	L6	45	L4 SAME L3	US-PGPUB; USPAT
7	L7	370	L1 NEAR6 L2	US-PGPUB; USPAT
8	L8	10	L7 SAME L3	US-PGPUB; USPAT